

Performance of systemic juvenile idiopathic arthritis classification criteria: One-center experience in Libya

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Abstract: Systemic juvenile idiopathic arthritis (sJIA) is an autoinflammatory disorder often presenting with prominent systemic features before arthritis develops. Classification criteria for sJIA have evolved, yet their comparative performance-especially in paediatric populations-remains underexplored in real-world settings. To evaluate and compare the performance of three classification criteria-ILAR (2004), PRINTO/ACR (2021), and Yamaguchi-in a paediatric cohort with suspected sJIA, with a focus on early diagnosis in the pre-arthritis phase. A retrospective cohort study was conducted at Tripoli Children's Hospital, Libya, including 38 patients treated for systemic inflammation between 2005 and 2020. Demographic, clinical, and laboratory data were extracted from medical records. Patients were classified according to ILAR, PRINTO/ACR, and Yamaguchi criteria. Agreement analysis, sensitivity, specificity, positive and negative predictive values, and kappa statistics were calculated, using PRINTO as the reference standard. The median age was 7.5 years (IQR 3.1-9.9), with nearly equal sex distribution. All patients presented with fever, 78.9% had evanescent rash, and 92.1% had arthritis at presentation. Yamaguchi criteria were met by only 36.8% of patients, showing poor sensitivity (36.1%) and agreement with PRINTO ($\kappa = 0.036$). ILAR criteria were fulfilled by 92.1%, but were missed in all three patients without arthritis. PRINTO criteria captured 94.7%, including one pre-arthritis case missed by ILAR. ILAR demonstrated high sensitivity (97.2%) and specificity (100%) against PRINTO, while Yamaguchi performed poorly across all metrics. The Yamaguchi criteria are inadequate for classifying paediatric sJIA. While ILAR criteria remain specific, they risk delaying diagnosis in peri-arthritis presentations. The PRINTO/ACR 2021 criteria offer a more sensitive and clinically useful framework for early classification of sJIA, supporting their adoption in paediatric practice to facilitate timely diagnosis and intervention.

Introduction

Juvenile idiopathic arthritis (JIA) unifies all forms of chronic childhood arthritis, affecting not only joints but also extra-articular structures, including eyes, skin, and internal organs, leading to disability and even associated fatality. It is defined as the presence of arthritis of unknown etiology that begins before the age of 16 and persists for at least 6 [1]. Juvenile idiopathic arthritis is the most common rheumatologic disease of childhood. JIA is classified by subtype according to the International League of Associations for Rheumatology criteria (ILAR). Depending on the number of joints affected, presence of extra-articular

manifestations, systemic symptoms, serology, and genetic factors, JIA is divided into oligoarticular, polyarticular, systemic, psoriatic, enthesitis-related, and undifferentiated arthritis [2]. The main characteristics of arthritis, internal organ involvement, genetic predisposition, laboratory markers of each subtype, and adult equivalent are shown in **Table 1**.

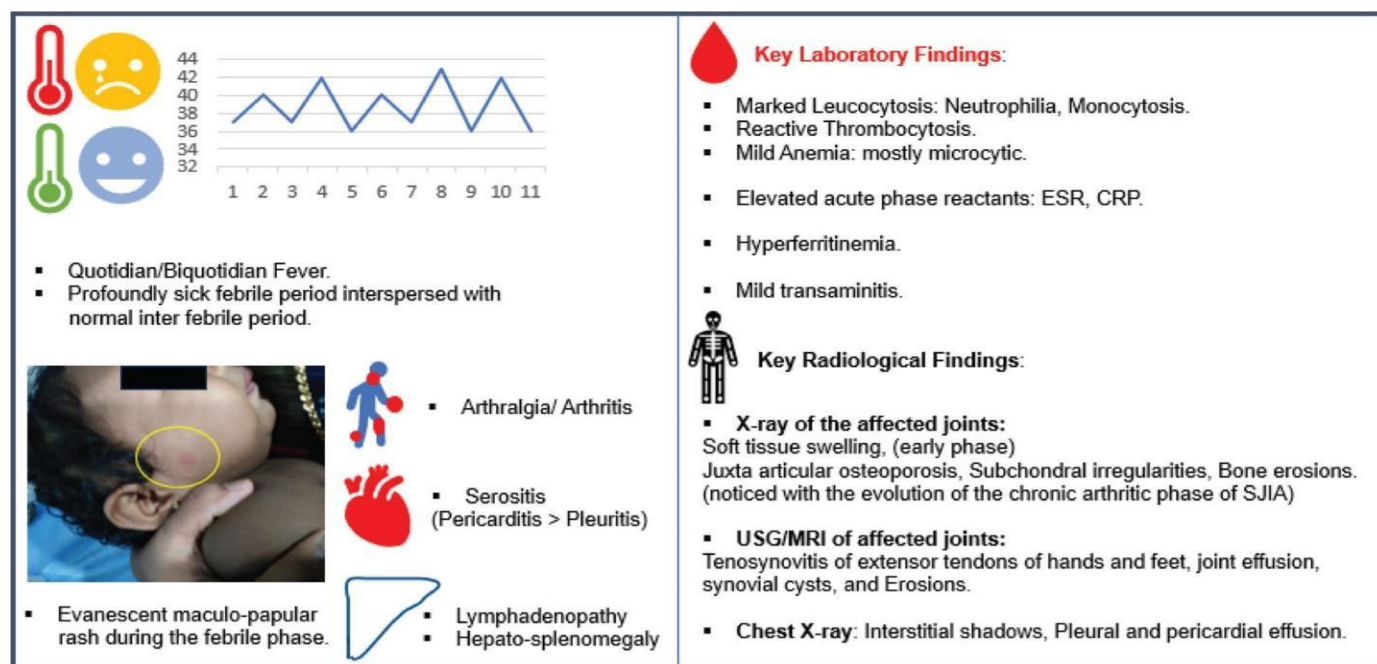
Table 1: IA subtypes based on the Juvenile idiopathic arthritis classification criteria

Subtype	Oligoarticular JIA	Polyarticular JIA RF-	Polyarticular JIA RF+	ERA	Psoriatic JIA	Systemic sJIA
Characteristic of arthritis	≤ 4 joints affected, mainly large joints Asymmetric, often only a single joint (knee)	≥ 5 joints affected, Symmetric or asymmetric Small and large joints Sometimes a cervical spine and/or temporomandibular joint	≥ 5 joints affected Symmetric Mainly small joints (metacarpophalangeal joints and wrists) Erosive Aggressive symmetric polyarthritis	Lower limb Joints are affected more commonly Axial involvement: sacroiliac joint, hip, or shoulder	Asymmetric Arthritis Small and large joints	Usually arthralgias; 30-50% of chronic arthritis - slowly developing Mostly wrists, knees, ankle joints or asymptomatic temporomandibular arthritis
Systemic manifestation	30.0% uveitis	10.0% uveitis	Rheumatoid nodules 10.0% uveitis	Acute anterior uveitis Enthesitis Gut inflammation	Psoriasis Dactylitis Onycholysis Nail pitting Uveitis (10%-15%)	Spiking fever Generalized lymphadenopathy Migratory salmon pink rash Serositis (pericarditis most common, then pleuritic and peritonitis) Hepatosplenomegaly MAS

Systemic Juvenile idiopathic arthritis (sJIA) accounts for approximately 10.0% of all types of JIA. But it has the most acute and severe disease and disproportionately high morbidity compared with other subtypes [2, 3]. This disease subtype, characterized predominantly by systemic symptoms, affects females and males with the same frequency and may occur at any time during childhood. The presence of arthritis and intermittent fever for at least two weeks plus one of the following defines the disease: typical rash, generalized lymphadenopathy, hepatosplenomegaly, or serositis [2]. Peak incidence is between one and five years of age, but sJIA can occur at any age. Disease with an onset after 16 years of age is called adult-onset Still's disease [AOSD], although the term "Still's disease" has been proposed to encompass this disease across age groups. SJIA is one of the most important differential diagnoses in a child presenting with pyrexia of unknown origin. It is prudent to suspect SJIA in any child presenting with an unexplained prolonged febrile episode with a typical pattern and associated symptoms as described below [3]. SJIA is characterized by a distinctive pattern of fever, characterized by temperature spikes crossing 39 °C once or twice a day with a rapid return to normalcy within a few hours. However, the classic pattern of fever is observed in around 37.0% of children. Evanescent, asymptomatic, erythematous macular or maculopapular rash distributed over trunk, neck, and proximal extremities is observed during peaks of temperature in more than 80.0% of children and resolves completely without residual scarring or pigmentation at fever defervescence. Hence, the rash may be easily missed in a dark-skinned child or, if not observed, during the peak of fever. Other less common cutaneous lesions include migratory non-pruritic erythema displaying Koebner phenomenon and urticarial lesions. Although arthritis is a mandate for meeting ILAR classification criteria for SJIA, arthralgia alone is commonly found at disease onset, and true arthritis evolves within weeks, months, or rarely years later (most commonly within three months of disease onset) [4, 5]. The pattern of arthritis may be variable, ranging from migratory oligoarticular to fixed polyarticular patterns. The most commonly involved joints include the wrist, knee, and ankle. The hip, cervical spine, temporomandibular joint, and small joints of the hands and feet are the other commonly affected joints [6]. Although serositis is mostly asymptomatic and is incidentally detected on imaging, acute pericarditis can be symptomatic, causing chest pain, and can evolve rapidly into cardiac

tamponade. Similarly, pleuritis is observed less frequently. Reticuloendothelial manifestations, generalized lymphadenopathy (in over 25.0% of children), and hepatosplenomegaly are less frequently observed during the active phase of the disease.

Figure 1: Clinical features of systemic juvenile idiopathic arthritis



When all the common clinical manifestations of sJIA are present, the diagnosis is relatively straightforward. However, frequently, only some are present at onset, so that the differential diagnosis becomes very broad and challenges even the most experienced clinician [7]. There may be a prolonged delay between the onset of fever and the development of arthritis, but according to the International League of Associations for Rheumatology (ILAR) criteria, a definitive diagnosis of sJIA cannot be made until arthritis is present and is shown to be persistent. However, these patients are often very ill and need urgent evaluation and treatment. Thus, any patient suspected of having sJIA should be referred as quickly as possible to a pediatric rheumatologist, if available, for their expert opinion and management. A pediatric rheumatologist may be able to make a diagnosis of probable sJIA and begin appropriate therapy before the required six weeks of symptoms and arthritis have elapsed, as long as other conditions have been ruled out [8].

Systemic juvenile idiopathic arthritis is unique within the JIA spectrum, considered more of an autoinflammatory disease. Its classification has evolved significantly to improve specificity and distinguish it from mimics. In comparison to the other diseases which are jointly grouped under the term JIA, sJIA or Still's disease, as it was previously known, has many distinct features. One important difference is that, at least in a subset of sJIA patients, arthritis may be a non-prominent and/or a delayed manifestation. Patients have been reported to have a delay of up to 10 years before the onset of arthritis. The International League Against Rheumatism (ILAR) criteria require the presence of arthritis to classify a patient as having sJIA. Since morbidity and mortality may develop early in sJIA patients, a strict adherence to the ILAR criteria may lead to an unacceptable delay in diagnosis [9].

The Yamaguchi criteria require the presence of five features, with at least two being major diagnostic criteria [10]. The four major Yamaguchi criteria are: Fever of at least 39 °C lasting at least one week, Arthralgia or arthritis lasting two weeks or longer, a non-pruritic macular or maculopapular skin rash that is salmon-colored in appearance and usually found over the trunk or extremities during febrile episodes, and Leukocytosis ($\geq 10,000/\text{microL}$), with at least 80.0% granulocytes. The minor Yamaguchi criteria include: Sore throat, lymphadenopathy, hepatomegaly or splenomegaly, abnormal liver function studies, particularly elevations in

aspartate and alanine aminotransferase and lactate dehydrogenase concentrations, and negative tests for antinuclear antibody (ANA) and rheumatoid factor (RF).

The ILAR classification criteria: It has been widely accepted. In addition to arthritis in any number of joints, these criteria include fever for at least two weeks (documented to be quotidian for three days) and at least one of the following features: evanescent, erythematous rash, generalized lymphadenopathy, serositis, and hepatomegaly or splenomegaly [11].

PRINTO 2019 classification criteria: Fever of unknown origin (excluding infectious, neoplastic, autoimmune, or monogenic autoinflammatory diseases) that is documented to be daily (quotidian; fever that rises to $\geq 39^{\circ}\text{C}$ once a day and returns to $\leq 37^{\circ}\text{C}$ between fever peaks) for at least three consecutive days and reoccurring over a duration of at least two weeks and accompanied by two major criteria OR one major criterion and two minor criteria. Major criteria are: evanescent (nonfixed) erythematous rash and arthritis. Minor criteria are: generalized lymph node enlargement and/or hepatomegaly and/or splenomegaly, serositis, arthralgia lasting two weeks or longer (in the absence of arthritis), and leukocytosis ($\geq 15,000/\text{mm}^3$) with neutrophilia [12].

Table 2: Classification criteria comparison

Feature	Yamaguchi Criteria	PRINTO/ACR 2021 Provisional Criteria (for sJIA)	ILAR 2004 Classification Criteria (for sJIA)
Core requirement	Fever of $\geq 39^{\circ}\text{C}$ for ≥ 1 week	Fever of ≥ 2 weeks' duration, documented to be quotidian for at least 3 days	Arthritis plus Fever of ≥ 2 weeks' duration, documented to be quotidian (daily) for at least 3 days
Major (Typical) Features	4 required, with arthralgia/arthritis ≥ 2 weeks: Fever $\geq 39^{\circ}\text{C}$, intermittent Arthralgia ≥ 2 weeks Typical rash (salmon-pink, evanescent) Leukocytosis ($\geq 10,000/\mu\text{L}$) with $\geq 80\%$ granulocytes	≥ 1 major feature + ≥ 2 minor features. Major: 1. Quotidian fever 2. Typical rash	Plus ≥ 1 of the following: 1. Evanescent rash 2. Generalized lymphadenopathy 3. Hepatomegaly/splenomegaly 4. Serositis
Minor (supportive) Features	3 required (if 5 majors are not met): 1. Sore throat	Minor (≥ 2 required): 1. Generalized lymphadenopathy	(Not structured as major/minor; see list in adjacent column)
	2. Lymphadenopathy 3. Hepatomegaly / splenomegaly 4. Abnormal LFTs 5. Negative ANA and RF	2. Hepatomegaly/splenomegaly 3. Serositis (pericarditis, pleuritis) Arthralgia (lasting ≥ 2 weeks) Note: Arthritis is not a required criterion	
Arthritis requirement	Arthralgia ≥ 2 weeks (can be arthritis)	NOT REQUIRED for classification	ABSOLUTELY REQUIRED
Exclusion criteria	Infections, malignancies, and another rheumatic diseases	Exclusionary Features: Psoriasis or a family history of HLA-B27+ male with arthritis onset > 6 yrs Positive RF on 2 occasions > 3 mo apart Presence of systemic lupus, dermatomyositis, etc	ILAR general exclusions: Psoriasis in patient/family HLA-B27+ male with arthritis onset > 6 yrs Positive RF Family history of HLA-B27 disease

The systemic symptoms of SJIA are often more significant at disease onset than arthritis, and the broad differential of fever of unknown origin can sometimes lead to misdiagnosis as an infectious disease [13]. Although distinct diagnostic criteria for SJIA exist, not all patients fulfill these criteria at onset.

Differential diagnoses of sJIA: The diagnosis of sJIA is largely clinical, so it is necessary to proceed by first excluding other serious systemic illnesses, such as infection and malignancy, before commencing the mainstay treatment. Malignancies, especially leukaemia and lymphoma [14]. Infections that may cause viral exanthema, such as measles, parvovirus, influenza, parainfluenza, herpes virus 6, Epstein-Barr virus, and cytomegalovirus, must be ruled out [15]. Differential diagnoses of arthritis, such as septic arthritis, post-infectious arthritis, rheumatic fever, transient synovitis, Lyme disease, and brucellosis, should be entertained when a child presents with fever and arthritis, as indicated by the case [16]. Other autoimmune and inflammatory conditions that may mimic sJIA to a great extent include systemic lupus erythematosus (SLE), KD, and other vasculitis diseases, periodic fever syndromes, and even other causes of HLH (familial or acquired) or immune deficiencies [17].

Table 3: Systemic juvenile idiopathic arthritis mimic

Mimickers of systemic juvenile arthritis	Examples
Infection	Abscesses or osteomyelitis: tuberculosis, brucellosis, EBV, CMV, parvovirus, measles, HIV
Malignancy	Leukemia or lymphoma
Autoimmune disease	SLE or polyarticular JIA with systemic manifestations
Vasculitis	KD or polyarteritis nodosa
Autoinflammatory periodic fever diseases	TNF receptor periodic fever
Immunodeficiencies	Especially those that may present with HLH

Systemic juvenile idiopathic arthritis can be difficult to diagnose because there are no specific diagnostic tests, and arthritis, which is necessary for definite diagnosis, is often not evident early in the course of the disease. In addition, infection, malignancies, and other diagnoses must be considered before the diagnosis of sJIA because these patients can present similarly with fever, rash, and joint pain. Many children with sJIA may have a delayed onset of arthritis and so fail to fulfil the ILAR criteria for sJIA. As Arthritis can be delayed in sJIA, using the ILAR criteria (which mandate arthritis) may delay diagnosis. The newer PRINTO criteria and the borrowed Yamaguchi criteria aim to identify patients earlier based on systemic symptoms. This study was undertaken to compare the performance of three classification criteria for sJIA in a pediatric population, particularly in the pre-arthritic phase: ILAR (2004) criteria: Requires the presence of arthritis. PRINTO/ACR (2021) Provisional criteria: Does not require arthritis. Yamaguchi criteria: Designed for adult-onset Still's disease but often used in children; it relies heavily on systemic features.

Materials and methods

Study design and period: Retrospective cohort study, as a cross-sectional study of the medical records of all patients diagnosed with SJIA, following up at the rheumatology clinic in Tripoli Children's Hospital.

Study setting: The study will be carried out in Tripoli Children's Hospital, which is one of the teaching hospitals providing tertiary health care services with a bed capacity of 150 beds, with several pediatric subspecialty clinics, including cardiology, endocrine, respiratory. Neurology. Gastroenterology. Metabolic, neonatology. Nephrology and rheumatology clinic; the latter (Rheumatology clinic) is the only government clinic offering pediatric rheumatology services covering all western and southern areas of Libya.

Study population: Pediatric patients diagnosed with systemic-onset juvenile idiopathic arthritis (sJIA) at Tripoli Children's Hospital, from 2005 to 2020.

Study tool: A preformed case sheet will be used to obtain the relevant data from the medical records, including the following: demographic data, clinical presentation, and inflammatory markers

Ethical considerations and consent process: An ethical approval will be obtained from the scientific committee and the head of Tripoli Children's Hospital before starting the study (003-42-MJ-2024).

Statistical analysis: The study will employ SPSS for statistical analysis, beginning with descriptive statistics (frequencies; mean $\pm$ SD or median [IQR]). Group comparisons will use Chi-square/Fisher's exact tests and t-test/Mann-Whitney U test.

Results

Cohort characteristics: A total of 38 pediatric patients treated for systemic inflammation were identified from the Tripoli Children's Hospital rheumatology clinic registry between 2005 and 2020. The demographic characteristics of the cohort are summarized in **Table 4**. The median age at presentation was 7.5 years (interquartile range [IQR] 3.1-9.9 years), with a range from 0.94 to 14.33 years. There was a nearly equal gender distribution (47.4% male [n = 18], 52.6% female [n = 20]). All patients presented with fever. The characteristic evanescent rash was present in 78.9% (30/38) of patients. Arthritis was documented at the initial presentation in 92.1% of the cohort, meaning that 7.9% presented in the pre-arthritic, purely systemic phase. The most common systemic features besides fever and rash were generalized lymphadenopathy (55.3%) and hepatomegaly and/or splenomegaly (15.8%). Serositis was present in 21.0% of patients, with pericarditis (18.4%) being more common than pleurisy (2.6%). 7.9% of patients had arthralgia without documented arthritis at presentation. Laboratory findings revealed marked leukocytosis ($\geq 10,000/\text{mm}^3$) in 76.3% of patients. Anemia (hemoglobin categorized as low) was present in 50.0% of patients, and thrombocytosis was observed in 68.4%. Inflammatory markers were frequently elevated: ESR was high in 86.8% of tested patients, CRP was high in 65.8%, and serum ferritin was elevated in 26.3% of those tested. Liver enzymes (ALT and AST) were predominantly within normal limits.

Table 4: Demographic and clinical characteristics of the study cohort

Characteristic	Result, n (%) or Median (IQR)
Demographics Total patients 38	
Age at presentation, years	
Median (IQR)	7.5 (3.1 - 9.9)
Range	0.94 - 14.33
Gender	
Male	18 (47.4%)
Female	20 (52.6%)
Clinical features at presentation	
Fever	38 (100%)
Evanescent Rash	30 (78.9%)
Arthritis Present	35 (92.1%)
Arthralgia (without arthritis)	3 (7.9%)
Generalized Lymphadenopathy	21 (55.3%)
Hepatomegaly/Splenomegaly	06 (15.8%)
Serositis	08 (21.0%)
Pericarditis	07 (18.4%)
Pleurisy	1 (2.6%)

Key laboratory findings

Leukocytosis ($\geq 10,000/\text{mm}^3$)	29 (76.3%)
Anemia (Low Hemoglobin)	19 (50.0%)
Thrombocytosis	26 (68.4%)
Elevated ESR (of tested, n=36)	33/36 (91.7%)
Elevated CRP (of tested, n=28)	25/28 (89.3%)
Elevated Ferritin (of those tested, n=15)	10/15 (66.7%)

Overall diagnostic performance of the three criteria sets: Classification criteria performance in the cohort: The analysis of the 38-patient cohort: Yamaguchi criteria: 14 patients (36.8%) met these criteria, meaning the majority (24 patients or 63.2%) did not fulfill them. ILAR 2004 Criteria: 35 patients (92.1%) fulfilled the criteria. The three patients (7.9%) who did not meet the ILAR criteria were those who lacked arthritis at presentation. PRINTO/ACR 2021 Provisional Criteria: 36 patients (94.7%) met these criteria. The high agreement with the ILAR criteria (92.1%) is likely because most patients (92.1%) already had arthritis at presentation. The key difference is that the PRINTO criteria captured one additional patient who was missed by ILAR, demonstrating its advantage in not requiring arthritis for classification.

Agreement analysis of classification criteria for sJIA: ILAR vs. PRINTO Agreement: There was very high agreement (35/38 cases). The single patient captured by PRINTO but not by ILAR represents the peri-arthritis case uniquely identified by the 2021 criteria. The PRINTO and ILAR criteria are not independent and demonstrate very strong agreement ($\Phi = 0.805$). Yamaguchi vs. Pediatric Criteria: Significant discordance exists. 22 patients (57.9% of the cohort) were classified as sJIA by both ILAR and PRINTO but did not meet the Yamaguchi criteria, indicating the latter's low sensitivity in this pediatric population.

Table 5: Overall diagnostic performance of the three criteria

Patient classification	Yamaguchi Met?	ILAR Met?	PRINTO Met?	Count (n)	% of Cohort	Clinical implication
Group A: Pediatric criteria consensus	No	Yes	Yes	22	57.9%	Classified by pediatric criteria but not by Yamaguchi (Low Yamaguchi sensitivity)
Group B: Full consensus	Yes	Yes	Yes	13	34.2%	Agreement across all three criteria sets.
Group C: PRINTO-unique capture	No	No	Yes	01	2.6%	Key finding: Captured only by PRINTO due to the absence of arthritis (pre-arthritic phase)
Group D: Yamaguchi-unique capture	Yes	No	No	01	2.6%	Met Yamaguchi criteria; potential false positive or atypical presentation

Performance metrics/against PRINTO standard: When using the PRINTO/ACR 2021 criteria as the reference standard, the ILAR 2004 criteria demonstrated excellent diagnostic performance with 97.2% sensitivity and 100% specificity. In contrast, the Yamaguchi criteria showed poor sensitivity (36.1%) while maintaining moderate specificity (50.0%). The positive predictive value was high for both criteria sets (Yamaguchi: 92.9%; ILAR: 100%), though the negative predictive value was notably low for Yamaguchi (4.2%) compared to ILAR (66.7%). Overall accuracy was 97.4% for ILAR versus 36.8% for Yamaguchi. The kappa statistic indicated poor agreement between Yamaguchi and PRINTO ($\kappa = 0.036$).

Table 5: Performance of Yamaguchi and ILAR criteria using PRINTO as the Gold Standard

Performance metric	Yamaguchi criteria	ILAR 2004 criteria
Sensitivity	36.1% (13/36)	97.2% (35/36)
Specificity	50.0% (1/2)	100% (2/2)
Positive Predictive Value (PPV)	92.9% (13/14)	100% (35/35)
Negative Predictive Value (NPV)	4.2% (1/24)	66.7% (2/3)
Accuracy	36.8% (14/38)	97.4% (37/38)
Kappa (agreement)	0.036 (Poor)	-0.111 (Poor)

Clinical profile non arthritis subgroup: All three patients without arthritis at presentation shared: Fever and rash at presentation (100%), male gender (100%), complications (100%), no hepatosplenomegaly (0.0%), No MAS at presentation (0.0%), lymphadenopathy present in 66.7%, laboratory findings varied (Hb 7.4 - 10.2 g/dL and WBC 7.2-12.5, etc.). The clinical phenotype of patients without arthritis is notable for universal fever, rash, and complications, suggesting these patients still have systemic disease despite lacking arthritis at presentation. In our cohort of 38 patients, 3 (7.9%) presented without arthritis. Among these, one (33.3%) was captured by PRINTO/ACR criteria, while none were captured by ILAR criteria. All three patients without arthritis exhibited fever and rash at presentation, and all developed complications. These findings suggest that ILAR criteria may exclude patients with systemic JIA who lack arthritis at presentation, whereas PRINTO/ACR and Yamaguchi criteria demonstrate greater sensitivity for this subgroup.

Criterion / Feature	Value	Percentage
Total without arthritis	3	100
PRINTO/ACR positive	1	33.3
Yamaguchi positive	1	33.3
ILAR positive	0	0.0

Discussion

This retrospective study evaluated the performance of three classification criteria for systemic juvenile idiopathic arthritis-the ILAR (2004), PRINTO/ACR (2021) provisional, and Yamaguchi criteria-in a pediatric cohort from a single tertiary center in Libya. Our findings highlight critical differences in sensitivity, specificity, and clinical applicability, with important implications for early diagnosis and management of sJIA. The majority of patients (92.1%) presented with arthritis, aligning with the classic phenotype of sJIA. However, a small but clinically significant subgroup (7.9%) presented in a pre-arthritic, purely systemic phase. The PRINTO/ACR 2021 criteria successfully captured all but two patients in the cohort, including the one pre-arthritic case missed by ILAR, underscoring its utility in early classification. In contrast, the Yamaguchi criteria demonstrated markedly low sensitivity (36.1%), classifying only one-third of the cohort, despite being frequently used in adult-onset Still's disease and sometimes applied to pediatric populations.

Our data strongly suggest that the Yamaguchi criteria, though valuable in adults, perform poorly in children. The low sensitivity (36.1%) and poor agreement with pediatric-specific criteria ($\kappa=0.036$) likely stem from several factors: differences in fever patterns, leukocytosis thresholds, and the prominence of extra-articular features in children. Furthermore, the Yamaguchi criteria require a combination of major and minor features that may not align with the early systemic presentation typical of pediatric sJIA [18]. These findings are consistent with prior studies questioning the transposition of adult classification tools to pediatric populations. Therefore, we advise against using Yamaguchi as a stand-alone tool for classifying sJIA in children. A central debate in sJIA classification has been whether arthritis should be mandatory for diagnosis. Our cohort included three patients without arthritis at presentation, one of whom was captured only by the PRINTO criteria. This

aligns with the growing recognition that sJIA is primarily an autoinflammatory disorder in which arthritis may be delayed or absent initially. The ILAR requirement for arthritis risks diagnostic delay, potentially postponing treatment during a critical inflammatory window. The PRINTO/ACR 2021 criteria, by contrast, allow classification based on systemic features alone, facilitating earlier recognition and intervention-a crucial advantage in preventing complications such as macrophage activation syndrome (MAS). The high diagnostic accuracy of the PRINTO criteria (94.7% classification rate) supports their adoption in clinical settings, particularly in regions with limited pediatric rheumatology expertise. Early classification can prompt timely referral, initiate appropriate investigations, and expedite treatment with IL-1 or IL-6 inhibitors, which have shown efficacy in systemic-onset disease. However, clinicians must remain vigilant to exclude mimics-such as infection, malignancy, and other autoinflammatory syndromes-since the PRINTO criteria are designed for classification, not diagnosis.

Our findings should be interpreted in light of several limitations. The single-center, retrospective design may introduce selection bias, and the small sample size-especially of pre-arthritic cases-limits statistical power. The cohort was drawn from a tertiary referral center, which may not fully represent the spectrum of sJIA in the community. Finally, laboratory testing (e.g., ferritin, cytokine profiles) was not uniformly available, which may affect the comprehensive application of criteria. Despite these limitations, this study provides real-world evidence from a setting with scarce pediatric rheumatology resources, highlighting the practical challenges of sJIA classification. The direct comparison of three major criteria sets in the same cohort strengthens internal validity. Our results support global efforts to update classification systems for sJIA, emphasizing the need for criteria that reflect its systemic and autoinflammatory nature.

Conclusion: This study demonstrates that the Yamaguchi criteria are inadequately sensitive for classifying sJIA in children and should not be used in paediatric practice. The ILAR criteria, while specific, miss pre-arthritic cases, potentially delaying diagnosis and treatment. The PRINTO/ACR 2021 provisional criteria offer a more balanced approach.

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